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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/636,826	08/14/2000	Eike Duweing	50615	8623

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/636,826	DUWEING ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55,59,60,62-73,90,91,95 and 101-120* is/are pending in the application.

4a) Of the above claim(s) *101-120* is/are withdrawn from consideration.

5)☒ Claim(s) *55,59,60,62-73,90 and 91* is/are allowed.

6)☒ Claim(s) *95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's submissions filed on August 22, 2005 and December 5, 2005 have been entered.

Claims 1-54, 56-58, 61, 74-89, 92-94 and 96-100 are cancelled.

Claims 55, 59-60, 62-73, 90-91, 95 and 101-120 are pending.

Claims 101-120 are withdrawn.

Claims 55, 70 and 95 are currently amended.

Claims 55, 59-60, 62-73, 90-91 and 95 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Election/Restrictions

Applicant requests consideration of claims101-120 withdrawn in the previous office action on the basis that group I uses all of the promoters and constructs recited in the withdrawn claims for expressing a heterologous gene under stress conditions in general, without regard to whether the stress is induced by the influence of salt or vulneration.

The claims remain withdrawn because vulneration induced stress conditions were not searched and examined as part of the originally elected invention. The search of a broad genus (stress conditions in general) does not necessarily include, and may in fact exclude, specific species (vulneration induced stress conditions, for example).

Claim Rejections - 35 USC § 112

Claim 95 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed April 20, 2005.

Applicant's arguments filed August 22, 2005 have been fully considered but they are not persuasive.

With respect to Acuto S. et al. (An element upstream from the human delta-globin-encoding gene specifically enhances beta-globin reporter gene expression in murine erythroleukemia cells. Gene. 1996 Feb 12;168(2):237-41), previously cited by the Examiner in support of the rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant points out that Acuto S. et al. teaches only a "polypyrimidine-rich sequence", not a "polypyrimidine stretch" consisting of merely Cs and Ts as claimed in claim 95 (reply page 3).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a polypyrimidine stretch "consisting of merely Cs and Ts") are not recited in the rejected claim(s). The term "polypyrimidine stretch" recited in claim 95 is not further limited, and reads on any length of multiple pyrimidine units, such as those taught by Acuto S. et al. Further, the polypyrimidine-rich sequence taught by Acuto S. et al. does contain stretches consisting of Cs and Ts (see O'Neill D. et al. A DNA-binding factor in adult hematopoietic cells interacts with a

pyrimidine-rich domain upstream from the human delta-globin gene. Proc Natl Acad Sci U S A. 1991 Oct 15;88(20):8953-7, page 8955 Fig. 3 and page 8956 column 2 first paragraph).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With respect to Becker N.A. et al. (Characterization of a polypurine/polypyrimidine sequence upstream of the mouse metallothionein-I gene. Nucleic Acids Res. 1998 Apr 15;26(8):1951-8), previously cited by the Examiner in support of the rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant points to Figures 5C and 5D where it is shown that the presence of the polypurine/polypyrimidine element in test promoters leads to at least a slight increase in promoter activity under noninduced conditions and a stronger increase under induced conditions, and Applicant maintains that the fact that the increase in promoter activity observed by Becker N.A. et al. is only moderate under tested conditions does not necessarily mean that the claimed promoter is not with a high probability suitable for the expression of heterologous genes in plant cells (reply page 3).

Applicant's observations are inapposite to the outstanding rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, which was predicated on a failure to describe a representative number of species falling within the scope of the claimed genus which encompasses DNA constructs comprising the promoter of SEQ ID NO:1 wherein any number of pyrimidine stretches of unspecified sequence and length

are inserted in any unspecified location into the promoter, nor the structural features unique to the genus.

Applicant also maintains that one of ordinary skill in the art has concrete hints regarding which precise sequences to use and where, and in this regard Applicant points to page 12 of the specification, which describes V-ATPase isoform A and c1 promoters as each having two pyrimidine stretches, and isoform c2 as having one pyrimidine stretch. Applicant also points to Yanaka N. et al. (Isolation and characterization of the 5'-flanking regulatory region of the human natriuretic peptide receptor C gene. Endocrinology. 1998 Mar;139(3):1389-400), who teach a pyrimidine stretch that has been mapped as being responsible for proximal promoter activity of the natriuretic peptide receptor C promoter. (reply page 4)

The Examiner maintains that the disclosed promoter sequences and the promoter of Yanaka N. et al. that natively comprise at least one pyrimidine stretch are not species representative of the claimed genus, because the claimed genus requires species having an insertion of at least one further pyrimidine stretch into the promoter. Further, the claimed genus sets no parameters for the sequence and length of the pyrimidine stretch, or for the location of insertion, such that the disclosed promoter sequences and the promoter of Yanaka N. et al. are not recognizable as representative species.

With respect to Maiti A.K. et al. (Poly purine.pyrimidine sequences upstream of the beta-galactosidase gene affect gene expression in *Saccharomyces cerevisiae.*
BMC Mol Biol. 2001;2(1):11. Epub 2001 Oct 8), previously cited by the Examiner in support of

the rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant interprets the results as teaching that beta-galactosidase expression for promoter constructs with promoters carrying a single copy of a polypurine pyrimidine sequence (42 units) is not 12 fold reduced in comparison to promoter constructs without purine pyrimidine sequence in the promoter region, but is 12 fold reduced in comparison to promoters with a duplex sequence (485 units see Fig. 3b and 3c). Applicant also maintains that the very high beta galactosidase expression in the presence of the duplex sequence can also be explained by the duplex control sequence having a string cis-acting transcriptional regulatory effect (reply page 5).

Applicant's observations are inapposite to the outstanding rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, which was predicated on a failure to describe a representative number of species falling within the scope of the claimed genus which encompasses DNA constructs comprising the promoter of SEQ ID NO:1 wherein any number of pyrimidine stretches of unspecified sequence and length are inserted in any unspecified location into the promoter, nor the structural features unique to the genus.

Claim 95 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the office action mailed April 20, 2005.

Applicant's arguments filed August 22, 2005 have been fully considered but they are not persuasive.

With respect to Acuto S. et al. (An element upstream from the human delta-globin-encoding gene specifically enhances beta-globin reporter gene expression in murine erythroleukemia cells. Gene. 1996 Feb 12;168(2):237-41), previously cited by the Examiner in support of the rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant points out that Acuto S. et al. teaches only a "polypyrimidine-rich sequence", not a "polypyrimidine stretch" consisting of merely Cs and Ts as claimed in claim 95 (reply page 3).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a polypyrimidine stretch "consisting of merely Cs and Ts") are not recited in the rejected claim(s). The term "polypyrimidine stretch" recited in claim 95 is not further limited, and reads on any length of multiple pyrimidine units, such as those taught by Acuto S. et al. Further, the polypyrimidine-rich sequence taught by Acuto S. et al. does contain stretches consisting of Cs and Ts (see O'Neill D. et al. A DNA-binding factor in adult hematopoietic cells interacts with a pyrimidine-rich domain upstream from the human delta-globin gene. Proc Natl Acad Sci U S A. 1991 Oct 15;88(20):8953-7, page 8955 Fig. 3 and page 8956 column 2 first paragraph).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With respect to Becker N.A. et al. (Characterization of a polypurine/polypyrimidine sequence upstream of the mouse metallothionein-I gene. Nucleic Acids Res. 1998 Apr 15;26(8):1951-8), previously cited by the Examiner in support of the rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant points to Figures 5C and 5D where it is shown that the presence of the polypurine/polypyrimidine element in test promoters leads to at least a slight increase in promoter activity under noninduced conditions and a stronger increase under induced conditions, and Applicant maintains that the fact that the increase in promoter activity observed by Becker N.A. et al. is only moderate under tested conditions does not necessarily mean that the claimed promoter is not with a high probability suitable for the expression of heterologous genes in plant cells (reply page 3).

Applicant's analysis is inconsistent with that of Becker N.A. et al., who teach that plasmids containing the MT-I R/Y sequence (pJ111 and pJ112) were not significantly different with respect to promoter activity when compared to a control plasmid lacking the MT-I R/Y sequence, that in the absence of metal induction all promoter constructs displayed similar activities, and that a slight increase in promoter activity was observed upon metal induction of cells with 2uM CdCl2 when the MT-I R/Y sequence was present (page 1956 column 1 first and full paragraph paragraphs and Figure 5C and D). Further, the Examiner maintains that the teachings of Becker N.A. et al. do support the assertion that inserting at least one further pyrimidine stretch of unspecified sequence and length into any unspecified location of SEQ ID NO:1 is unpredictable, given that Acuto S. et al., Becker N.A. et al. and Maiti A.K. et al.

observed different effects when inserting different pyrimidine stretches into different promoter regions.

Applicant also maintains that one of ordinary skill in the art has concrete hints regarding which precise sequences to use and where, and in this regard Applicant points to page 12 of the specification, which describes V-ATPase isoform A and c1 promoters as each having two pyrimidine stretches, and isoform c2 as having one pyrimidine stretch. Applicant also points to Yanaka N. et al. (Isolation and characterization of the 5'-flanking regulatory region of the human natriuretic peptide receptor C gene. Endocrinology. 1998 Mar;139(3):1389-400), who teach a pyrimidine stretch that has been mapped as being responsible for proximal promoter activity of the natriuretic peptide receptor C promoter. (reply page 4)

The Examiner maintains that Applicant's disclosure of three promoter sequences and the promoter of Yanaka N. et al. do not provide sufficient guidance for one of ordinary skill in the art to practice the full scope of the claimed invention, which does not limit the length or sequence or position or number of pyrimidine stretches that may be inserted into SEQ ID NO:1.

With respect to Maiti A.K. et al. (Poly purine.pyrimidine sequences upstream of the beta-galactosidase gene affect gene expression in *Saccharomyces cerevisiae.*
BMC Mol Biol. 2001;2(1):11. Epub 2001 Oct 8), previously cited by the Examiner in support of the rejection of claim 95 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant interprets the results as teaching that beta-galactosidase expression for promoter constructs with promoters carrying a single copy of a polypurine

pyrimidine sequence (42 units) is not 12 fold reduced in comparison to promoter constructs without purine pyrimidine sequence in the promoter region, but is 12 fold reduced in comparison to promoters with a duplex sequence (485 units see Fig. 3b and 3c). Applicant also maintains that the very high beta galactosidase expression in the presence of the duplex sequence can also be explained by the duplex control sequence having a string cis-acting transcriptional regulatory effect (reply page 5).

Applicant's analysis is inconsistent with that of Maiti A.K. et al., who teach that the presence of the poly pur.pyr sequence in the plasmid causes a reduction in beta-galactosidase expression during derepression (column 4 last paragraph). The Examiner also maintains that the beta-galactosidase expression for promoter constructs with promoters carrying a polypurine pyrimidine was reduced in comparison to BOTH a promoter construct without a purine pyrimidine sequence in the promoter region (pLGSDS36), AND a promoter construct having a duplex sequence in the same location as the polypurine pyrimidine sequence in the test constructs (pAMDC61) (Figure 3; Materials and Methods Design and Cloning of poly pur.pyr stretch with a loop sequence). The Examiner further maintains that Maiti A.K. et al. teach that no marked differences were observed in the beta-galactosidase enzyme activities in cells containing pLGSDS36 (no purine pyrimidine sequence in the promoter region) and pAMDC61 (duplex sequence in the same location as the polypurine pyrimidine sequence in the test constructs) (column 4 last paragraph).

Allowable Subject Matter

Claims 55, 59-60, 62-73 and 90-91 are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Primary Examiner
Art Unit 1638

CC

Cynthia Collins

2/13/06